REMARKS

In the Final Action dated May 19, 2003, claims 4-8, 10-13 and 26-29 are pending and under consideration. Claims 4-6, 8, 10-11 and 26-27 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent No. 5,801,142 to Zain et al. Claims 12 and 13 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over the '142 patent in view of U.S. Patent No. 6,167,888 to Tuszynski et al. Claims 7 and 28-29 are objected to as dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

This Response addresses each of the Examiner's rejections and objections. Applicants therefore respectfully submit that the present application is in condition for allowance or at least in better condition for appeal. Favorable consideration of all pending claims is therefore respectfully requested.

With respect to the §102(b) rejection, the Examiner states that the '142 patent teaches that the mouse Mts1 protein migrates on a gel with a molecular weight of 10-12 kD. See, e.g., column 38, lines 50-52 and Figure 15 of the '142 patent. The Examiner further states that the '142 patent teaches that the human Mts1 protein has an apparent molecular weight of 27 kD. See Figure 16 and column 38, lines 53-58 of the '142 patent. The Examiner reasons that, since there is a difference of only 7 amino acids between the mouse and human sequences, it appears that the 27 kD band identified in Figure 16 is a trimeric form of human Mts-1. Thus, the Examiner concludes that the '142 patent appears to teach an isolated trimeric form of Mts-1, anticipating the instant claims.

Applicants respectfully submit that the Examiner's conclusion that the 27kD band

represents an isolated trimeric form of Mts-1 is ill-founded. In this connection, Applicants provide herewith a Declaration (**Exhibit 1**) by Dr. Eugene Lukanidin, a co-inventor named in the present application and in the '142 patent. Dr. Lukanidin explains in the Declaration, that Figure 16 of the '142 patent depicts a Western blot analysis of serum samples obtained from normal women and patients with breast carcinomas or advanced malignant lymphomas. Dr. Lukanidin further explains that the protein band with an apparent molecular weight of approximately 27 kD observed in the Western blot apparently contained denatured human Mts1 polypeptide, because the band was detected by α-mts1 antibodies, but disappeared (i.e., competed off) when the Western blot was probed with α-mts1 antibodies in the presence of free mts-1 protein.

However, Applicants respectfully submit that because the serum samples were run on a 12% SDS-PAGE gel (i.e., under denaturing conditions), this Mts1-containing 27kD material are composed of denatured polypeptides and is not expected to have any biological activity. In addition, there is no indication anywhere in the '142 patent that the 27 kD band contains multiple Mts1 polypeptides. As Dr. Lukanidin explains in Paragraph 7 of the Declaration, the 27 kD band merely represents an aggregate of denatured proteins. The aggregate could be an aggregate containing one or more denatured Mts1 polypeptides, or an aggregate containing one denatured Mts1 polypeptide in combination with other polypeptides present in the serum sample. In contrast, the multimeric Mts1 complex, as disclosed and claimed in the present application, is composed of undenatured Mts1 proteins and has neurogenic activity. Moreover, the specification demonstrates that a multimeric Mts1 complex, isolated according to the present invention, appears as an 11 kD band on an SDS-PAGE (i.e., under denaturing conditions). See Figure 11D and page 37, lines 25-30 of the '509 application.

Therefore, Applicants respectfully submit that the 27kD band disclosed in the '142 patent by no means equates to the multimeric Mts1 complex as presently claimed. Assuming, *pro arguendo*, that the 27 kD band contains multiple Mts1 molecules, the 27kD band is not a material isolated or purified to any degree. As Dr. Lukanidin explains in Paragraph 8 of the Declaration, the 27 kD band was merely detected in the Western blot as a component among numerous proteins present in the serum sample. There was simply no recovery of the 27 kD material, i.e., no isolation of the 27 kD material, away from other components in the serum sample. In contrast, the present claims are directed to an isolated multimeric Mts-1 complex. As exemplified in Example 3, the paragraph bridging pages 36-37 of the present specification, an multimeric Mts-1 complex can be isolated by a chromatography procedure.

Applicants further respectfully submit that it is a unique recognition by the present inventors that Mts1 proteins form multimers and that the neurogenic activity of Mts1 proteins are associated with the multimeric forms of the protein, as opposed to the monomeric form and dimeric form of the protein. See, e.g., the paragraph bridging pages 36-37; and page 38, lines 4-17. There is no teaching or suggestion in the '142 patent that Mts1 proteins form multimers, let alone a suggestion to isolate a multimeric Mts1.

Accordingly, it is respectfully submitted that the '142 patent does not teach isolated multimeric Mts1 protein complexes, as presently claimed. Withdrawal of the rejection under §102 based on the '142 patent is respectfully requested.

With respect to the rejection under 35 U.S.C. §103(a), the Examiner contends that the '888 patent teaches that bFGF, NGF, CNTF, BDNF, NT3, NT4, and IGF-I are neurotrophic factors, and that some of these factors stimulate growth of nerve cells and therefore can be used

to treat spinal cord injury. The Examiner concludes that it would have been *prima facie* obvious to one of ordinary skill in the art to combine the teachings of the '142 patent with the '888 patent to arrive at the pharmaceutical compositions of claims 12-13.

Applicants respectfully submit that neither the '142 patent nor the '888 patent teaches or suggests an isolated multimeric Mts1 protein complex, which is a requisite component of the pharmaceutical compositions of claims 12-13. Therefore, the pharmaceutical compositions of claims 12-13 are not obvious in view of the '142 patent and the '888 patent. Withdrawal of the §103 rejection based on the '142 patent in view of the '888 patent is therefore respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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Enc.: Exhibit 1 (Declaration of Dr. Eugene Lukanidin)